

CASE REPORTS

• Simple Management of Lead Poisoning

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DESPITE INCREASED RECOGNITION of the dangers of exposure and the availability of many methods of protection, lead poisoning is still one of the most important industrial diseases. The conventional therapeutic approach "demands much medical ingenuity," and specific therapy, often necessitating hospitalization, may have to be given for four to six weeks.⁴

In conventional therapy, large amounts of calcium are given at first, frequently by vein, to displace the bone-migrating lead ion. The continuing routine also usually includes magnesium sulfate catharsis, and finally a low calcium regimen to liberate the stored lead.

Several useful medical applications have already been found for the recently developed industrial cationic agents which form strong, nonionizing soluble chelate complexes with divalent and trivalent metals.^{1, 6, 8, 9, 13} Ethylene diamine tetraacetic acid (EDTA) has been reported to bring about hypocalcemia and reduced systemic calcium levels in humans and to have no noxious effects. It has been used to dissolve ordinarily insoluble salts such as calcium oxalate, barium sulfate and lead phosphate, and indeed has been successfully used to dissolve urinary calculi.^{1, 6} The preformed compound, calcium ethylene diamine tetraacetic acid, possesses the potential of having its calcium displaced by other metals. Results of experiments with animals suggested that the complex would be of potential value in the management of heavy metal poisonings by withdrawing the metal in a soluble excretable form and replacing it with calcium in the storage reservoir. To date an increasing body of information affirms that this new agent is probably the most innocuous specific therapeutic device available in the detoxication of lead and several radioactive ions. Several reports of use of the drug in the treatment of lead and mercury poisoning have already appeared.^{2, 3, 7, 10, 11, 12} Following is a case report

illustrative of the use of this agent in lead intoxication.

REPORT OF A CASE

A 32-year-old woman was admitted to the hospital on March 22, 1953, with complaint of generalized abdominal pain that had begun about a month previously and had become progressively more severe until it was of colicky character. It was accompanied by intermittent nausea and vomiting and alternating constipation and diarrhea. All the symptoms became more severe and about March 15 the pain became almost continuous. The patient was unable to eat or sleep, had malaise and weakness and remained in bed. The weight decreased about 10 pounds in several weeks. Several physicians who had been consulted diagnosed several types of "enteritis" and prescribed antibiotics, which were ineffective.

Since July 1952 the patient had been employed part-time at a ceramics works as a sprayer of underglaze.* In January 1953 she took a full-time job elsewhere in the same capacity. In the second job, unlike the first, she was not issued a protective face mask, and a blower used to clear the spray fumes was disconnected because it was "noisy." After several weeks she noted that nasal secretions were heavily coated with the pigment that was being sprayed. When she vomited early in the present illness, she noted that the vomitus contained large amounts of the pigments.

The lead content in a 24-hour specimen of urine† on March 20 was more than 0.5 mg. per liter (normal up to 0.08 mg. per liter) and the amount of lead in the blood was 0.365 mg. per 100 cc. (normal up to 0.05 mg.).

On physical examination the patient appeared to be in acute distress, sitting flexed or upright and clutching the abdomen and moaning. The temperature was 98 degrees F., the pulse rate 90 and respirations 28 per minute. The abdomen was round

* Underglaze as applied to ceramics usually consists of an aqueous suspension of "frit" mixed with silica, a pigment of colored oxides, clay and organic gums. The "frit" is a commercial ground mixture of melted raw materials which usually contains lead, averaging perhaps 30 to 40 per cent but as much as 70 per cent. Although the underglaze spray in its final form may contain no lead at all, usually the lead content ranges from 5 to 20 per cent.

† Analyses to determine the content of lead in the blood and the urine were done in the Spectrographic Laboratory of the School of Medicine, University of Southern California, by the method of Butt and associates. Determinations were done in triplicate. Average deviation on each sample based on reproducibility was less than 4 per cent. (Butt, E. M., Nusbaum, R. E., Gilmour, T. C., and Di Djo, S. L.: The use of the emission spectrograph for the analysis of biological materials, to be published.)

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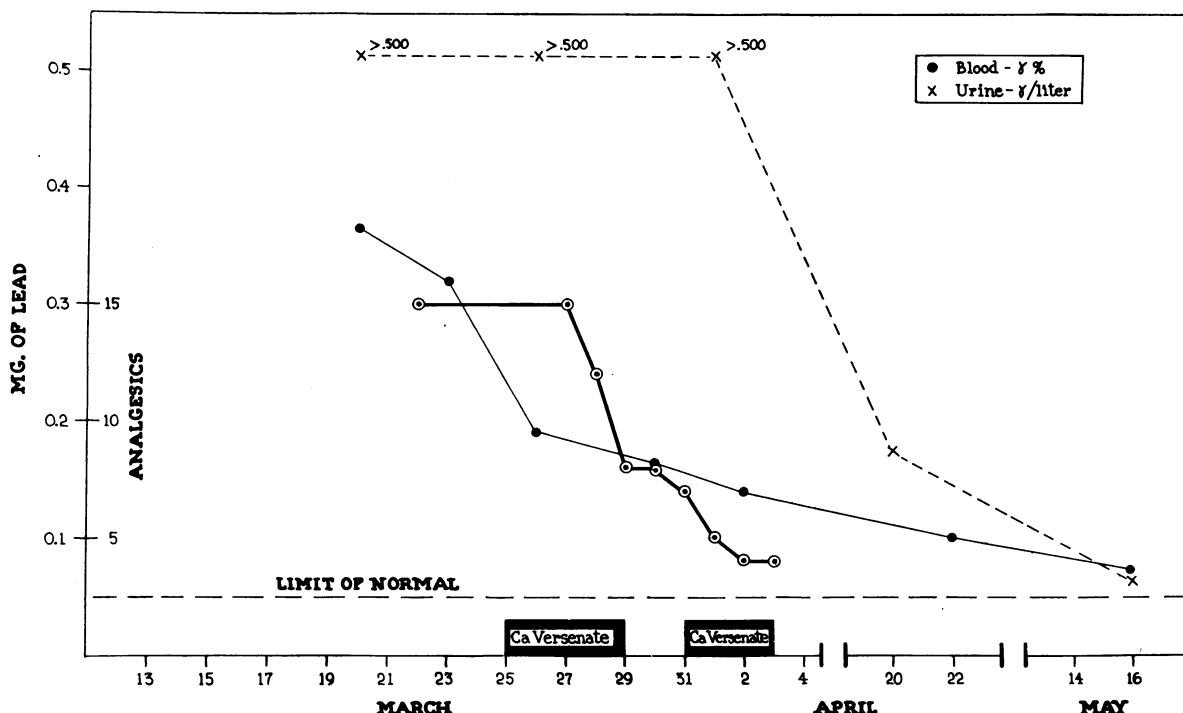


Chart 1.—Effect of intravenous administration of calcium disodium versenate on the content of lead in the blood (mg. per 100 cc.) and in the urine (mg. per liter) of a patient with lead intoxication. The rating of "analgesics" is an expression of the total daily doses of sedatives and analgesics required to keep the patient comfortable.

and soft. Spasm was not noted. There was only mild generalized tenderness.

Laboratory: Erythrocytes numbered 3.8 million per cu. mm. of blood and the hemoglobin content was 8.8 gm. per 100 cc. Leukocytes numbered 10,350 per cu. mm.—62 per cent polymorphonuclear cells, 30 per cent lymphocytes, 8 per cent eosinophils, 0.8 per cent reticulocytes, and 1.4 per cent basophilic stippled erythrocytes. No abnormalities were noted in the urine. Results of chemical studies of the blood were within normal limits. In roentgen studies after barium enema the only abnormality observed was delayed emptying. X-ray films of the chest were normal.

At first, therapy consisted of a conventional regimen of a high calcium diet supplemented with calcium gluconate orally, magnesium sulfate once daily, and atropine sulfate. To relieve the distress and pain, barbiturate sedation was maintained continuously and morphine and codeine sulfate were given alternately, each two or three times daily. On March 25 treatment with calcium disodium versenate (calcium EDTA) was begun[‡]; 2 gm. in 1 liter of 5 per cent glucose in saline solution was given intravenously over a 6 to 8-hour period. Similar infusions were given on all but one of the next ten days. Within four days after administration of calcium disodium versenate was begun, the patient was symptomatically improved with reduction in pain. The content of lead in the blood decreased

rapidly, while the amount in the urine remained high during the phase of increased excretion (Chart 1). She was discharged from the hospital April 3 but, as noted in the chart, laboratory examination of blood and urine was carried out several times thereafter. At the time of discharge a high intake of calcium gluconate and ferrous sulfate was prescribed. By April 18 the hemoglobin had increased to 12 gm. per 100 cc. of blood and by June 6 it was 13.5 gm. The postrecovery course was uneventful save for an episode of acute alcoholism apparently stemming from emotional instability which may have arisen from effects of lead intoxication on the central nervous system.

DISCUSSION

The administration of the calcium-binding ethylene diamine tetraacetic acid by intravenous drip has been used by the author in ten cases to reduce the amount of calcium in the serum. Reduction of as much as 50 per cent, to near tetanic levels, has been observed.⁵ The amount of calcium to be bound and excreted was easily calculated and verified by examination. No toxic phenomenon other than minor venospastic pain in the cannulated vessel was observed when as much as 2 gm. was administered at one time.⁵

The nontoxic nature of the preformed calcium ethylene diamine tetraacetic acid has been emphasized in the several reports of its successful use in

[‡]The calcium versenate was supplied by Riker Laboratories, Inc., Los Angeles.

the treatment of poisoning with mercury, lead and other heavy metals.^{2, 3, 7, 10, 11, 12} It has been given orally as well as intravenously with good effect.¹¹

Since the binding of calcium in the chelate complex is relatively weak, in vitro, the calcium can be displaced by many metals such as lead, cobalt, nickel, chromium and copper. The chelation follows a definite order which varies for given divalent or trivalent ions within the pH of the solution.¹⁰ However, in vivo, the calcium-metal exchange occurs with less uniformity because of active complexing agents in the body which form stronger metal bonds than does the calcium EDTA. Treatment of poisoning caused by lead, cobalt and nickel has been favorably influenced, and it has also been reported that symptomatic improvement was obtained when EDTA was used in mercury poisoning.¹⁰ Other studies in which quantitative determinations were better than in the present case have also shown that the administration of calcium EDTA results in pronounced enhancement of lead excretion and rapid subsidence of the symptoms of lead intoxication.

Thus, the cumbersome and prolonged therapy of the past can now be entirely replaced by the use of calcium EDTA (or calcium versenate) in doses of 1 to 2 gm. daily in an intravenous drip for rapid excretion of the body-stored lead and relief of associated symptoms. The drug can also be administered orally, although the excretion of lead is slower.

SUMMARY

In the treatment of a patient with lead poisoning resulting from exposure to material used in the underglaze of ceramics, a new chelating agent, calcium

disodium versenate, was used. It rapidly removed the free and bound lead from the blood.

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